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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,384	RIDDER ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-34 (in part), drawn to methods for discriminating dysplastic cells from non-dysplastic cells by assaying for the presence of a nucleic acid.

Group II, claims 1-34 (in part), drawn to methods for discriminating dysplastic cells from non-dysplastic cells by assaying for the presence of a polypeptide.

Group III, claims 1-34 (in part), drawn to methods for discriminating dysplastic cells from non-dysplastic cells by assaying for the presence of a nucleic acid and a polypeptide.

Group IV, claims 35-38 (in part), drawn to kits comprising reagents to detect a nucleic acid.

Group V, claims 35-38 (in part), drawn to kits comprising reagents to detect a polypeptide.

Group VI, claims 35-38 (in part), drawn to kits comprising reagents to detect a nucleic acid and reagents to detect a polypeptide.

2. The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A 371 case is considered to have unity of invention only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression “special technical feature” means

those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. However, the technical feature linking the inventions, and particularly the technical feature of invention IV was known in the art at the time the invention was made. For example, Riethdorf (Human Pathology. 2002. 33: 899-904; cited in the IDS of April 28, 2005) teaches nucleic acid probes for detecting p16INK4a and Ki67. The probe for p16INK4a constitutes a reagent for detecting the expression of a INK4a gene product, and the probe for Ki67 constitutes a reagent for detecting a cell proliferation marker gene product (see page 890). Note that in the absence of any recitation in the claims or any direction provided in the specification to the contrary, the recitation of kit reads on component parts capable of being assembled or a plurality of elements grouped together as a kit. Accordingly, the word "kit" does not impart any additional special structural or functional features which distinguishes the claimed kits over the reagent compositions of Riethdorf. Thus, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

3. **Further restriction requirement applicable to invention I-VI**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

I. p16INK4a

II. p14ARF

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

With respect to inventions I-III, claim 4 encompasses species I and II.
With respect to inventions IV-VI, claim 36 encompasses species I and II.

The following claim(s) are generic:
claims 1-3 and 5-34, with respect to inventions I-III;
claims 35 and 37-38, with respect to inventions IV-VI.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acids and proteins differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species I and II do not share both a common structure and activity as is required to show that they are of a similar nature.

4. **Further restriction requirement applicable to inventions I-III**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

I. cell proliferation marker for senescence;

II. a marker for terminal cell differentiation;

III. a marker for apoptosis; and

IV. a marker for cell cycle arrest

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claims 1-34 encompass species I-IV

No claims are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited

nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species I-IV do not share both a common structure and activity as is required to show that they are of a similar nature.

5. **Further restriction requirement applicable to inventions I-III**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

I. cell proliferation proliferation marker necessary for the maintenance of cell proliferation;

II. a proliferation marker engaged in DNA replication;

III. a proliferation marker being or encoding a member of the processive replication fork;

IV. a senescence marker;

V. a cell cycle arrest marker; and

VI. an apoptosis marker.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. The election of a species selected from species I-VI must be consistent with the species election in paragraph 4 above.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claims 5-10 encompass species I-VI

Claims 1-4 and 11-34 are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species I-IV do not share both a common structure and activity as is required to show that they are of a similar nature.

6. **Further restriction requirement applicable to inventions I-III**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

Ki67, Ki-S5, Ki-S2, MCM2, MCM3, MCM4, MCM5, MCM6, MCM7, HELAD1, CDC6; CDC7 protein kinase, Dbf4, CDC14 protein phosphatase, CDC45, MCM10, PCNA, and POLD

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. The election of a species selected from the species recited above must be consistent with the species election in paragraph 4 and 5 above.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claims 6-10 encompass the species listed above.

Claims 1-5 and 11-34 are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species listed above do not share both a common structure and activity as is required to show that they are of a similar nature.

7. **Further restriction requirement applicable to inventions I-III**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

I. senescence marker;
II. an apoptosis marker;
III. a cell cycle arrest marker;
IV. a marker for terminal differentiation of cells;
V. a marker for viral infection;
VI. a marker for viral activity;
VII. a cell cycle regulatory protein;
VIII. a gene-product necessary for the maintenance of cell proliferation;
IX. a gene-product engaged in DNA replication; and
X. a gene product being a member of the processive replication fork.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claims 14 encompasses species I-X

Claims 1-13 and 15-34 are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species I-X do not share both a common structure and activity as is required to show that they are of a similar nature.

8. **Further restriction requirement applicable to inventions I-III**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

I. HPV16
II. HPV18
III. HPV31
IV. HPV33;
V. HPV35;
VI. HPV39;
VII. HPV45;
VIII. HPV51;
IX. HPV52;
X. HPV56;
XI. HPV58;
XII. HPV59;
XIII. HPV66; and
XIV. HPV68

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply

must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claim 18 encompasses species I-XIV

Claims 1-17 and 19-34 are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, species I-X do not share both a common structure and activity as is required to show that they are of a similar nature.

9. **Further restriction requirement applicable to inventions IV-VI**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of the following:

CDC6, MCM3, MCM3, MCM4, MCM5, MCM6, MCM7, CDC7 protein kinase, Dbf4, CDC14 protein phosphatase, CDC45 and MCM10, Ki67, Ki-S2, PCNA and POLD.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claim 37 encompasses the species listed above.

Claims 35-36 and 38 are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acid and protein markers differ from each other with respect to their nucleotide and amino acid sequences, respectively, and differ in their functional activities. Thereby, the species listed above do not share both a common structure and activity as is required to show that they are of a similar nature.

10. **Further restriction requirement applicable to inventions IV-VI**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a particular combination of:

a. a pl6INK4a sample for carrying out a positive control reaction;

b. a p 14ARF sample for carrying out a positive control reaction;

c. a Ki67 sample for carrying out a positive control reaction;

d. a Ki-S2 sample for carrying out a positive control reaction;

e. an MCM5 sample for carrying out a positive control reaction;

f. an MCM2 sample for carrying out a positive control reaction;

g. a PCNA sample for carrying out a positive control reaction;
h.reagents for detection of the presence or absence and/or the level ofpl6INK4a;
i.reagents for detection of the presence or absence and/or the level ofpl4ARF;
j. reagents for detection of the presence or absence and/or the level of Ki67;
k. reagents for detection of the presence or absence and/or the level of Ki-S2;

l. reagents for detection of the presence Or absence and/or the level of MCM5;
m. reagents for detection of the presence or absence and/or the level of MCM2
n. reagents for detection of the presence or absence and/or the level of PCNA;

o. one or more samples oflNK4a gene-products for carrying out positive control reactions;

p. one or more samples of cell proliferation marker gene-products for carrying out positive control reactions;

q. one or more reagents for the detection of the presence or absence and/or the level of other INK4a gene products; and

r. and one or more reagents for the detection of the presence or absence and/or the level of other cell proliferation marker gene products.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply

must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. The election of a species or a combination of species selected from species a) – r) must be consistent with the species election in paragraphs 3 and 9 above.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claim 38 encompasses the species listed above.

Claims 35-37are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited reagents for detecting nucleic acid and protein markers differ from each other with respect to structure, such as their nucleotide and amino acid sequences, with respect to their functional activities and effects. Thereby, species a)- r) listed above do not share both a common structure and activity as is required to show that they are of a similar nature.

11. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be

traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

/Carla Myers/
Primary Examiner, Art Unit 1634